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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,468	11/27/2006	Paolo Morazzoni	2503-1225	5191

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EXAMINER	
MI, QIUWEN	
ART UNIT	PAPER NUMBER
1655	

NOTIFICATION DATE	DELIVERY MODE
12/30/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DocketingDept@young-thompson.com

Office Action Summary	Application No.	Applicant(s)	
	10/587,468	MORAZZONI ET AL.	
	Examiner	Art Unit	
	QIUWEN MI	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23 and 26-46* is/are pending in the application.

4a) Of the above claim(s) *43-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,26-42 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 July 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment in the reply filed on 12/20/2010 is acknowledged, with the cancellation of Claims 1-22, 24, and 25. Claims 23, and 26-46 are pending. Claims 43-45 are withdrawn. **Claims 23, 26-42 and 46 are examined on the merits**.

Any rejection that is not reiterated is hereby withdrawn.

Claim Rejections –35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 23, 26, 29-40, and 46 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Physiologics (Physiologics, Physphatidylserine complex with Ginkgo, 2003, online document provided as IDS by Applicant on 7/27/2006), in view of Bombardelli (EPA 0275005) (provided as IDS by Applicant on 7/27/2006).

This rejection is maintained for reasons of record set forth in the Office Action mailed out on 8/19/2010, repeated below. Applicants' arguments filed have been fully considered but they are not deemed to be persuasive.

Physiologics teaches dietary supplement of 60 softgels (thus in the form of capsules/gels, thus the limitation of claim 30 is met, thus for oral administration, thus the limitation of claim 31 is met). Physiologics teaches phosphatidylserine complex with Ginkgo biloba is perfect for mild memory problems associated with aging (thus a method for the enhancement of cognitive function and alleviation of mental fatigue by improving the speed of memory and memory quality, by counteracting cognitive fatigue in normal and healthy persons, thus a method for the treatment of a disease related with the reduction of cognitive function, such as dementia or Alzheimer's disease). Physiologics teaches phosphatidylserine plays a role in neurotransmissions and supports cognitive function while Ginkgo biloba helps improve memory (col 1, 1st paragraph). Physiologics teaches phospholipid complex from soy lecithin standardized to contain 20% phosphatidylserine, 100 mg (thus a phospholipid containing 10-50%, 20-40%, or 20% of phosphatidylserine, thus the limitations of claims 23-25 are met). Physiologics teaches the product containing Ginkgo biloba extract 30 mg (standardized to contain 24% Ginkgo flavone glycosides) (thus at least 20% Ginkgo flavone) (3rd column, Supplement Facts). Thus the ratio between Ginkgo and the phosphatidylserine is about 1:3 (thus the limitations of claims 29 and 46 are met). Physiologics also teaches the product comprising 5 mg vitamin C (3rd column, Supplement Facts) (thus a pharmaceutically acceptable amount of at least one additive selected from vitamins, thus the limitation of claims 33 and 34 are met).

Physiologics does not teach forming a complex between Ginkgo and phosphatidylserine; neither does Physiologics teach the claimed dosage in claim 32.

Bombardelli teaches complex compounds of flavonoids with phospholipids, characterized by high lipophilia and improved bioavailability and therapeutic properties as compared with free,

not complexed flavonoids. The complex compounds of the invention are suitable for use as the active principle in pharmaceutical and cosmetic (see Abstract). Bombardelli also teaches complex compounds of flavonoids with phospholipids (claim 1), wherein the phospholipids are selected from phosphatidyl serine, etc (claim 4), and wherein the flavonoids are selected from the group consisting of ginkgonetine, isoginkgonetine and bilobetine (claim 5), etc (thus Ginkgo biloba extract). Bombardelli also teaches the invention also provides a process for purifying flavonoids from plants such for example as Ginkgo biloba etc (page 3, 6th paragraph). Bombardelli further teaches the preparation of ginkgo biloba depurated extract /total soy phospholipids complex (page 10, Example 11).

It would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to form a complex of Ginkgo biloba extract with phosphatidylserine in Physiologics since Bombardelli teaches complex of flavonoids and phospholipids has high lipophilia and it improves bioavailability; Bombardelli also teaches the preparation of ginkgo biloba extract and soy phospholipids complex as an example. Therefore, it would have been obvious for one of the ordinary skill in the art to form complex of Ginkgo biloba extract with soy phospholipid containing 20% phosphatidylserine in Physiologics to improve bioavailability so as to enhance cognitive function and alleviate of mental fatigue.

Regarding the limitation to the claimed dosage in claim 32, the result-effective adjustment in conventional working parameters is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan. It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. The differences in concentration or

temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). see MPEP § 2144.05 part II A. Although the prior art did not specifically disclose the claimed dosage in claim 32, it would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine the dosage of phosphatidylserine complex with Ginkgo biloba because the amount of the claimed

components is art-recognized result effective variables because it has the ability enhance memory function, which would have been routinely determined and optimized in the pharmaceutical art.

From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is prima facie obvious over the references, especially in the absence of evidence to the contrary.

Claims 23, 26-41, and 46 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Physiologics and Bombardelli as applied to claims 23, 26, 29-40, and 46 above, and further in view of Loew (Value of Ginkgo biloba in treatment of Alzheimer dementia, Wiener medizinische Wochenschrift (1946), (2002) Vol. 152, No. 15-16, pp. 418-22. Ref: 40).

This rejection is maintained for reasons of record set forth in the Office Action mailed out on 8/19/2010, repeated below. Applicants' arguments filed have been fully considered but they are not deemed to be persuasive.

The teachings of Physiologics and Bombardelli are set forth above and applied as before.

The combination of Physiologics and Bombardelli do not specifically teach the principle active substance of Ginkgo biloba extract is bilobalide, the Ginkgo extract contains 2-10% terpene lactones, or the incorporation of acetylcholinesterase inhibitor into the composition.

Loew teaches Ginkgo biloba special extract Egb 761 is a standardized and highly purified extract of Ginkgo leaves. Among the active constituents are the ginkgo-flavone glycosides and the terpene-lactones (ginkgolides, bilobalide). The presence of these constituents in Ginkgo

extracts, which constituents are known to be useful for treating Alzheimer's disease, provides the rationale for clinical trials in vascular dementia and primary degenerative dementia of the Alzheimer's disease, and in mixed forms of both. In clinical trials of different working-groups, effects of Ginkgo biloba on the cognitive performance, global function, and activities of the daily living have been found. Metaanalysis in the indication—dementia disorders--comparing Ginkgo biloba versus acetylcholinesterase inhibitors have shown a similar clinical efficacy of both therapy regimens with an additional drug safety benefit for Ginkgo. Loew further teaches that clinical trials with fixed combinations of acetylcholinesterase inhibitors with Ginkgo biloba extracts in moderate or severe demantia would be necessary (see Abstract).

It would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to use the ginkgo-flavone glycosides and 2-10% terpene-lactones (ginkgolides, bilobalide) from Loew in the enhancement of cognitive function as Loew explicitly teaches Ginkgo biloba extract contains those components. It would have been prima facie obvious for one of ordinary skill in the art to include acetylcholinesterase inhibitors in the composition since Loew teaches Ginkgo biloba has shown a similar clinical efficacy with acetylcholinesterase inhibitors, and clinical trials with fixed combinations of acetylcholinesterase inhibitors with Ginkgo biloba extracts in moderate or severe demantia would be necessary (see Abstract).

From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is prima facie obvious over the references, especially in the absence of evidence to the contrary.

Claims 23, 26, 29-40, 42, and 46 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Physiologics and Bombardelli as applied to claims 23, 26, 29-40, and 46 above, and further in view of Kim et al (Kim et al, Proteomics of neuroprotective actions of grape seed extract, FASEB Journal, (March 2003) Vol. 17, No. 4-5, pp).

This rejection is maintained for reasons of record set forth in the Office Action mailed out on 8/19/2010, repeated below. Applicants' arguments filed have been fully considered but they are not deemed to be persuasive.

The teachings of Physiologics and Bombardelli are set forth above and applied as before.

The combination of Physiologics and Bombardelli do not specifically teach the incorporation of grape seed extract into the composition.

Kim et al teach certain botanicals are purported to have health benefits because of anti-oxidant activity intrinsic to their polyphenol content. Grape seed extract (GSE) preparations, enriched in the proanthocyanidins, are in this category. Animal behavior studies showed that dietary supplementation with blueberry extract, enriched in proanthocyanidins similar to those in GSE, protected against age-related cognitive decline (see Abstract).

It would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to incorporate the grape seed extract from Kim et al into the composition of Physiologics since Kim et al teach Grape seed extract (GSE) preparations, enriched in the proanthocyanidins, protected against age-related cognitive decline. Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to

incorporate the grape seed extract from Kim et al into the composition of Physiologics for the enhancement of cognitive function.

From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is prima facie obvious over the references, especially in the absence of evidence to the contrary.

Applicant argues that "The Office Action takes the position that PhysioLogics teaches a composition comprising phospholipid complex that contains 20% phosphatidylserine and Gingko biloba extract that is advertised to treat mild memory problems associated with aging. What the Office Action does not recognize, however, is that the PhysioLogics product "Phospatidylserine Complex with Ginkgo" is not a Ginkgo-phospholipid complex that is the subject matter of the present claims. The PhysioLogics product advertised in the document is merely a mixture of a Gingko biloba extract and a phospholipid complex, i.e., it is not Gingko complexed with phospholipids. This is an important distinction between the composition of the present claims and that of PhysioLogics and other products that may have been available in the prior art. The PhysioLogics product is not a Ginkgo-phospholipid complex as defined in the specification" (page 9, last paragraph). Applicant also argues that "The ingredients listed in PhysioLogics includes Neuro- PSTH which is "phospholipid complex from soy lecithin". The phospholipid complex contains phosphatidylserine, phosphatidic acid, phosphatidylinositol, soy phospholipids & glycerides, phosphatidylcholine and phosphatidylethanolamine. (See, also document from Neuro PS website (http://www.neuropsocom) in the Appendix. A second

separately listed ingredient is Gingko biloba extract. The PhysioLogics compound is recognized for containing phosphatidylserine, which plays a role in neurotransmission and supports cognitive function, and containing Ginkgo biloba, which helps improve memory" (page 10, last paragraph). Applicant further argues that "The presently claims are directed essentially to methods for enhancing cognitive function and alleviating mental fatigue, improving memory speed and memory quality, or treating disease related to reduced cognitive function and increased mental fatigue. The methods comprise administering Ginkgo complexed with phospholipid and/or phosphatidylserine. As described in the specification, Applicants unexpectedly found that a Ginkgo biloba extract complexed with phosphatidylserine can be used to enhance cognitive function and alleviate mental fatigue significantly above the levels provided by the non- complexed extract (see, page 3, lines 16-20 of the International PCT application). As described in the specification, the Ginkgo- phosphatidylserine complex can be obtained from a reaction of the active ingredients of an extract of Ginkgo with a phospholipid containing 20% phosphatidylserine (see page 5, lines 10-14). The specification further details the preparation of a complex between the Ginkgo biloba and phosphatidylserine (see page 6, lines 14-21)" (page 11, 1st paragraph). Applicant argues that "The formation of Ginkgo phospholipid complexes enables the preparation of new biologically active compositions. In fact, they possess physico-chemical and spectroscopic characteristics which are markedly different from those of the original components and as such they can be incorporated as active principals into pharmaceutical formulations. For example, Ginkgo shows a strong affinity for phospholipids, resulting in the generation of bonds which markedly modify the physico-chemical and spectroscopic

characteristics of these new molecules (see page 6, lines 22-29)" (page 11, last paragraph bridging page 12).

This is not found persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). As evidenced by Physiologics, it is recognized by the art that phosphatidylserine complex with Ginkgo biloba is perfect for mild memory problems associated with aging, Physiologics also teaches the claimed concentration of (20%) of the complex. Even though the formation of the phosphatidylserine complex with Ginkgo biloba in Physiologics is not exactly the same as described in the current Specification, the second reference Bombardelli teaches complex compounds of flavonoids with phospholipids.

Applicant argues that "BOMBARDELLI describes compounds combining flavenoids with phospholipids. BOMBARDELLI discloses that flavenoids possess a number of recognized properties such as anti- inflammatory, antispasmodic, antihistaminic, vasodilatory and platelet antiaggregating. The flavenoids can be applied topically but flavenoids are also known to be poorly absorbed. Thus, BOMBARDELLI addresses this problem by preparing compounds by reacting a flavenoid in an aprotic solvent with a phospholipid to form a complex compound which is then isolated" (page 12, 2nd paragraph). Applicant also argues that "BOMBARDELLI fails to teach or suggest, however, that flavenoids would have any effect on the enhancing cognitive function or alleviating mental fatigue, or for improving memory speed and memory quality, or for treating any disease related to reduced cognitive function and increased mental

fatigue, which is the featured subject matter of the present claims. Furthermore, BOMBARDELLI fails to recognize that a Ginkgo biloba extract complexed with phosphatidylserine has significant effects above the non-complexed extract" (page 12, 3rd paragraph). Applicant further argues that "The specification shows, in the cognitive assessment tests and results, that Ginkgo biloba extract complexed with phosphatidylserine has outstanding effectivity compared with other tested species (i.e. non-complexed Ginkgo or Ginkgo phosphatidylcholine complex), regarding Quality of Memory, Picture Recognition Accuracy, Speed of Memory, Timed Memory Tasks, and other tasks concerning attention (see page 16, line 16 to page 29, line 5, and Figures 1-6). Further support for the unexpectedly superior results of a Ginkgo-phosphatidylserine complex was provided in the Rule 132 Declaration of Ezio Bombardelli, already of record. See, Amendment dated May 29, 2009" (page 12, last paragraph bridging page 13). Applicant argues that "BOMBARDELLI, however, fails to teach or suggest to one of ordinary skill in the art to form a Gingko-phospholipid complex and use this complex in a method for enhancing cognitive function and alleviating mental fatigue, or any of the other methods recited in the present claims" (page 13, 2nd paragraph).

This is not found persuasive. Bombardelli teaches complex compounds of flavonoids with phospholipids, characterized by high lipophilia and improved bioavailability and therapeutic properties as compared with free, not complexed flavonoids. The complex compounds of the invention are suitable for use as the active principle in pharmaceutical and cosmetic (see Abstract). Bombardelli also teaches complex compounds of flavonoids with phospholipids (claim 1), wherein the phospholipids are selected from phosphatidyl serine, etc (claim 4), and wherein the flavonoids are selected from the group consisting of ginkgonetine, isoginkgonetine

and bilobetine (claim 5), etc (thus Ginkgo biloba extract). Bombardelli also teaches the invention also provides a process for purifying flavonoids from plants such for example as Ginkgo biloba etc (page 3, 6th paragraph). Bombardelli further teaches the preparation of ginkgo biloba depurated extract /total soy phospholipids complex (page 10, Example 11). It would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to form a complex of Ginkgo biloba extract with phosphatidylserine in Physiologics since Bombardelli teaches complex of flavonoids and phospholipids has high lipophilia and it improves bioavailability; Bombardelli also teaches the preparation of ginkgo biloba extract and soy phospholipids complex as an example. Therefore, it would have been obvious for one of the ordinary skill in the art to form complex of Ginkgo biloba extract with soy phospholipid containing 20% phosphatidylserine in Physiologics to improve bioavailability so as to enhance cognitive function and alleviate of mental fatigue.

Applicant's arguments have been fully considered but they are not persuasive, and therefore the 103 rejections in the record are maintained.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Qiuwen Mi whose telephone number is 571-272-5984. The examiner can normally be reached on 8 to 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Qiuwen Mi/

Primary Examiner, Art Unit 1655